

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Budowsky, et al.  
Serial No: ---  
Confirmation No: ---  
Filed: Herewith  
For: METHODS AND COMPOSITIONS FOR THE SELECTIVE  
MODIFICATION OF NUCLEIC ACIDS

Examiner: Unknown  
Art Unit: Not yet assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF  
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed before the mailing date of a first Office Action on the merits in the above-identified case.

No fee or certification is required.

PART II: Information Cited

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

The Applicant hereby makes the following additional information of record in the above-identified application.

PART III: Explanation of Non-English Language References and Remarks Concerning Other Information Cited

The following is a concise explanation of the relevance of each non-English language reference listed on the attached form PTO-1449 (modified):

The following are remarks concerning the other information cited:

PART IV: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.


By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,  
*Edward Budowsky, et al., Applicant*

  
John R. Van Amsterdam, Reg. No. 40,212  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2211  
Telephone: (617) 720-3500

Docket No. V0191.70036US00  
Date: September 9, 2003

<b>FORM PTO-1449/A and B (Modified)</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				APPLICATION NO.: ---		DOCKET NO.: V0191.70036US00			
				FILING DATE: Herewith		CONFIRMATION NO.: ---			
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				GROUP ART UNIT: not yet assigned		EXAMINER: Unknown			
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#### U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
	*A1	US 3,487,157		Pierce, et al.	12/30/1969
	*A4	US 5,547,576		Onishi, et al.	08/20/1996
	*A5	US 5,691,132		Wollowitz, et al.	11/25/1997
	*A6	US 5,891,705		Budowsky, et al.	04/06/1999
	*A9	US 6,114,108		Budowsky	09/05/2000
	*A10	US 6,136,586		Budowsky	10/24/2000
	*A11	US 6,143,490		Cook, et al.	11/07/2000
	*A12	US 6,171,777		Cook, et al.	01/09/2001
	*A13	US 6,177,441		Cook, et al.	01/23/2001
	*A16	US 6,410,219		Cook, et al.	06/25/2002
	*	US 5,559,250		Cook et al.	09/24/1996
	*	US 5,374,424		Kelsey et al.	12/20/1994
	*	US 5,232,844		Horowitz et al.	08/03/1993
	*	US 5,120,649		Horowitz et al.	06/09/1992
	*	US 5,055,485		Geacintov et al.	10/08/1991
	*	US 5,000,951		Bass et al.	03/19/1991
	*	US 4,841,023		Horowitz	06/20/1989
	*	US 4,058,599		Bauer et al.	11/15/1997
	*	US 4,036,952		Bauer et al.	07/19/1977
	*	US 3,492,289		Richard H. Symm et al.	01/27/1970
	*	US 3,626,196		Amaudin et al.	12-1971
	*	US 4,567,042		Acree et al.	01-1986
	*	US 4,429,045		Bass et al.	01-1984

#### FOREIGN PATENT DOCUMENTS

Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	*B1	EP	EP 0 476 711	A2, A3	Nakai, et al.	03/25/1992	
	*B2	JP	JP 6-805520	A	Ohwada, et al.	03/22/1994	Yes
	*B3	WO	WO 96/14737	A1	Cook, et al.	05/23/1996	
	*B4	WO	WO 97/07674	A1	Budowsky, et al.	03/06/1997	
	*B6	WO	WO 98/45415	A1	Budowsky, et al.	10/15/1998	
	*B7	JP	55-009056	A1	Shigematsu et al.	01/22/1980	Yes (abst.)
	*	WO	96/39818		PCT	12/19/1996	

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		Office/Country	Number	Kind Code			
	*	EP	0612532	A2	Europe	08/31/1994	
	*	SU	594771	A1	Soviet Union; English translation	07/07/1993	Yes
	*	WO	92/18161		PCT	10/29/1992	
	*	SU	178636	A1	Soviet Union; English translation	10/15/1992	Yes
	*	RO	101400		Romania; English abstract	04/12/1992	Yes
	*	WO	92/03157		PCT	03/05/1992	
	*	JP	53-82735		Japan		
	*		009655595		Abstract only	10/15/1992	
	*		010096757		Abstract only	07/07/1993	

#### OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)	
	*C2	Atwell, G.J. et al.. "Synthesis, DNA Interactions and Biological Activity of DNA Minor Groove Targeted Polyberizamide-linked Nitrogen Mustards," Bloorg Med. Client. 1995 Jun; 3(6):679-91		
	*C3	Briel, S. et al Identification of New Aqueous Chemical Degradation Products of Isophosphoramidate Mustard J Pharm Biomed Anal. 2001 Jun;25 (3-4): 669-78.		
	*C4	Budowsky, E.I., "Problems and prospects for preparation of killed antiviral vaccines" Adv. Virus Res. 39:255-90 (1991)		
	*C5	Charache, S. et al.. "Evaluation of Extracorporeal Alkylation of Red Cells as a Potential Treatment for Sick Cell Anemia," Blood 1976; 47(3):481-88		
	*C6	Danao, T. et al., "Nitrogen Mustard as Induction Therapy for Rheumatoid Arthritis: Clinical and Immunologic Effects." J. Rheum. 1992 19:1683-86		
	*C7	Drake, M.E. et al., "Effect of Nitrogen Mustard on Virus of Serum Hepatitis in Whole Blood." Proc. of Soc. Exp. Bio. Med. 1952(80)310-13		
	*C8	Ferguson, L.R. et al.. "DNA-directed Aniline Mustards with High Selectivity for Adenine or Guanine Bases: Mutagenesis in a variety of Salmonella Typhimurium Strains Differing in DNA-Repair Capability," Mutat Res. 1994 Apr; 321(1-2):27-34		
	*C9	Ferguson, L.R. et al.. "Bacterial Mutagenicity Studies of DNA-Intercalating Aniline Mustards: an Insight Into the Mode of Action of a Novel Class of Anti-Tumor Drugs," Anticancer Drug Des. 1989 Oct; 4(3):209-19		
	*C10	Fries, K.M. et al 31P NMR and Chloride Ion Kinetics of Alkylating Monoester Phosphoramidates J. Med. Chem 1991 Feb;34(2): 565-9		
	*C11	Gao, Yi-Gui; Sriram, M. et al.. "Minor Groove Binding of SN6999 to an Alkylated DNA: Molecular Structure of d(CGC[e6G]AATTCGCG)-SN6999 Complex," Biochemistry 1993, Sep 21; 32(37):9639-48		

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Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
	*C12	Gourdie T.A. et al.. "DNA-directed Alkylating Agents. 1. Structure-activity Relationships for Acridine-linked Aniline Mustards: Consequences of Varying the Reactivity of the Mustard," J. Med. Chem. 1990 Apr; 33(4):1177-86	
	*C13	Gourdie T.A. et al.. "Synthesis and Evaluation of DNA-targeted Spatially Separated Bis(Aniline Mustards) as Potential Alkylating Agents with Enhances DNA Cross-linking Capability," J. Med. Chem. 1991 Jan; 34(1):240-8	
	*C14	Gravatt, G.L. et al.. "DNA-directed Alkylating Agents. 6. Synthesis and Antitumor Activity of DNA Tumor Groove-targeted Aniline Mustard Analogues of Pibenzimol," J. Med. Chem.. 1994 Dec. 9; 37(25): 4338-45	
	*C15	Gravatt, G.L. et al.. "DNA-Directed Alkylating Agents 4. 4-Anilinoquinoline-Based Minor Groove Directed Aniline Mustards," J. Med Chem 1991, 34(5):1552-60	
	*C16	Griffin M.T. et al Kinetics of Activation and in Vivo Muscarinic Receptor Binding of N-(2-bromoethyl)-4-Piperidiny Diphanylacetate: an Analog of 4-DAMP Mustard J. Pharmacol Exp Ther 1993 Jul; 266(1) 301-5.	
	*C17	Hamza, A. Quantum Molecular Modeling of the Interaction Between Guanine and Alkylating Agents—2-Nitrogen Mustard J. Biomol Struct Dyn 1996 Jun; 13(6):915-24	
	*C18	Hartman, F.W. et al., "Preparation and Sterilization of Blood Plasma." Ant. J. Clin. Path, 1954(24); 339-48	
	*C19	Hartman, F.W. et al.. "On the Chemical Sterilization of Blood and Blood Plasma." Proc. of Soc.. Exp. Bio. Med. 1949;70:248-54	
	*C20	Hartman, F.W., et al.. "Four-Year Study Concerning the Inactivation of Viruses in Blood and Plasma," Presented at the 55th Annual Meeting of the American Gastroenterological Association, San Francisco, California, June 1954	
	*C22	Hemminki, K. "DNA Adducts of Nitrogen Mustards and Ethyleneimines" DNA Adducts: Identification and Biological Significance, IARC Scientific Publications No. 125, Editors: Hemminki, et al., 1994, pp. 313-321.	
	*C23	Hemminki, K. Reactions of Nitrogen Mustards with DNA IARC Sci. Publ 1986; (78):55-70	
	*C24	Knorre, D.G. et al.. "Reactive Derivatives Of Oligonucleotides As Potential Antiviral Drugs," Problems of Virology, 1985, No.5, pp. 524	
	*C25	Kohn, K.W. et al Mechanisms of DNA Sequence Selective Alkylation of Guanine-N7 Positions by Nitrogen Mustards Biochem Pharmacol 1988 May 1; 37(9): 1799-800	
	*C26	Lee, M et al., "In Vitro Cytotoxicity of GC Sequence Directed Alkylating Agents Related to Distamycin," J. Med. Chem. 1993, Apr 2; 36(7)863-70	
	*C28	LoGrippe, G.A et al.. "Chemical and Combined Methods for Plasma Sterilization. , 6th Congress of the Int'l Soc. of Blood Trans., 1958, pp. 225-230	
	*C29	Mattes, W.B. et al.. "GC-rich Regions in Genomes as Targets for DNA Alkylation," Carcinogenesis 1988; 9(11):2065-72	
	*C30	Prakish, A.S. et al., "Differences in Sequence Selectivity of DNA Alkylation by Isomeric Intercalating Aniline Mustards," Chem. Biol. Interact. 1990; 76(23):241-8	
	*C31	Price, C.C. et al Relative Reactivities for Monofunctional Nitrogen Mustard Alkylation of Nucleic Acid Components Biochim Biophys Acta 1968 Sep 24; 166(2):327-59	
	*C32	Roth, E.F. Jr. et al., "Metabolic Effects of Antisickling Amounts of Nitrogen and Nor-Nitrogen Mustard on Rabbit and Human Erythrocytes." Blood 1975;45(6):779-88	

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	*C33	Springer, J.B. et al Isophosphoramidate Mustard and Its Mechanism of Bisalkylation J. Org. Chem 1998 Oct. 16; 63(21):7218-7222	
	*C34	Valu, K.K. et al., "DNA-directed Alkylating Agents. 3. Structure-activity relationships for Acridine-linked Aniline Mustards: Consequences of Varying the Length of the Linker Chain." J. Med. Chem 1990 Nov; 33(11):3014-9	
	*C35	Verschaeve, L. et a. "Mutagenicity of Ethyleneimine" Mutation Res. 238:39-55 (1990)	
	*C36	Vlasov, V.V. et al., -The Feasibility, Of Blocking Influenza Infections By Means Of Alkylating Derivatives Of Oligonucleotides," Molecular Genetics, Microbiology, And Virology, 1984, No. 11	
	*C37	Warrington, "Derivatives of Aziridine as Inactivants for Foot-and-Mouth Disease Virus Vaccines" Am J. Vet. Res., Vol. 34, No. 8. pp. 1087-1091	
	*C38	Wickham, G. et al., "DNA-binding Properties and Antitumour Activity of Monofunctional Alkylating Groups Attached to the DNA-intercalating Chromophore Phenanthridine: n-Bromoalkylphenanthridinium Bromides," Biochimic et Biophysica Acta 1991 1073:528-37	
	*C39	Wilke, W.S. et cal., "Parenteral Nitrogen Mustard for Inflammatory Arthritis," C'lev. Clin. J. Med. 1990 Oct; 57(7):643-46	
	*C40	Yamamoto, et al. Cancer Research 26, pt. 1, 2301-2306 (Nov 1966)	
	*C41	Yang, C. et al The Preparation of an Inactivated Antigen for Bluetongue Serology Zentralbl Veterinarmed [B] 1984 May; 31(4); 290-6.	
	*	Bahnmann, H.G., "Inactivation of Viruses in Serum with Binary Ethyleneimine," Journal of Clinical Microbiology, Vol. 3, No. 2, pp. 209-210 (1975).	
	*	Bahnmann, H.G., "Inactivation of Viral Antigens for Vaccine Preparation with Particular Reference to the Application of Binary Ethyleneimine," Vaccine, 8:299-303 (1990).	
	*	Budowsky, et al., "Inactivation of the phage MS2 infectivity by the action of ethyleneimines," Biorg. Khim. 11:989-991 (1985) (in Russian). English Abstract provided, 1 page.	
	*	Budowsky, E.I. and Zaleskaya, M.A., "Principles of selective inactivation of viral genome. v. Rational selection of conditions for inactivation of the viral suspension infectivity to a given extent by the action of B-propiolactone," Vaccine 9:319-325 (1991).	
	*	Budowsky, E.I. et al., "Principles of Selective Inactivation of the Viral Genome; Dependence of the Rate of Viral RNA Modification on the Number of Protonizable Groups in Ethyleneimine Oligomer", Vaccine Research, 50(1)29-39 (1996).	
	*	Creech et al., "Antitumor and Mutagenic Properties of a Variety of Heterocyclic Nitrogen and Sulfur Mustards," Medicinal Chemistry, 15:739-746 (1972).	
	*	Dermer, O.C. and Ham, G.E., Ethyleneimine And Other Aziridines, Acad. Press, NY - London (1969), pp. 249285.	
	*	Earley, J.E et al., "Reactions of Ethyleneimines. IX. The Mechanisms of Ring Openings of Ethyleneimines in Acidic Solutions," J. Am Chem. Soc. 80:3458-3462 (1958).	
	*	King, "Evaluation of Different Methods of Inactivation of Newcastle Disease Virus and Avian Influenza Virus in Egg Fluids and Serum," Avian Diseases 35:505-514 (1991).	
	*	Kochetkov, N.K. and Budowsky, E.I. eds., Organic Chemistry of Nucleic Acids, Part A, Plenum Press, London-New York, pp. 48-55, (1972).	
	*	Kostyanovskii et al., "Oligomers of aziridines and N-beta-azridinoethylamides, " Bulletin of the Academy of Sciences of the USSR, Division of Chemical Science Vol. 37(11):2315-2325, 20	

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		May 1989. (Translated from Izvestiya Akademi Nauk SSSR, Senya Khimicheskaya 11:2566-2575.)	
	*	Prodouz et al., "Inhibition of Merocyanine 540-mediated Photosensitization of Platelets and Viruses," Transfusion 31:415-422 (1991).	
	*	Race, E. et al., "An Experimental Chemically Inactivated HIV-1 Vaccine induces Antibodies that Neutralize Homologous and Heterologous Viruses", Vaccine, 13(1): 54-60 (1995).	
	*	Tanirbergenov, T.B. et al., "Regularities of mutagenic and toxic effects of ethyleneimine and its oligomers. A comparative study in the automated system SOS, hromotest and in standard bacterial test systems," Genetika 24:763 (1988) (in Russian). English translation provided, 5 pages.	
	*	Van Etten, R.L. and Dolhum, J.J., "Effects of Hydrogen-Bond Formation by Phenols on the Conformational Equilibrium of trans- 1,2-Dimethyl-3-isopropylaziridine," J. Org. Chem. 33:3904-3907 (1968).	
	*	Wagner et al., "Approaches to the Reduction of Viral Infectivity in Cellular Blood Components and Single Donor Plasma," Transfusion Med. Rev. V:18-32 (1991).	
	*	Zalesskaya, M.A., "Inactivation of viral genome by beta-propiolactone and ethyleneimines using the bacteriophage MS-2 as an example" dissertation presented 1988, in Moscow (M., 1988), degree conferred on May 4, 1989 (IH&. 05.04.89), catalogued in the Russian State Library (formerly the Lenin State Library).	
	*	Lobastov, A.E. pp. 4-6 in Probl. Virusol., Mol. Biol. Gistol. S-kh Zhivoten, Belov, A.D. ed., Mosk. Vet. Akad. Moscow, USSR, 1983	
	*	Hassanain, M.M. Revue Elev. Med. Vet. Pays Trop., 45/3-4:231-234, 1992.	
	*	Amor et al. (Journal of Medical Virology 19:367-376, 1986.	

EXAMINER	DATE CONSIDERED
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 09/609,687, filed July 5, 2000, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).